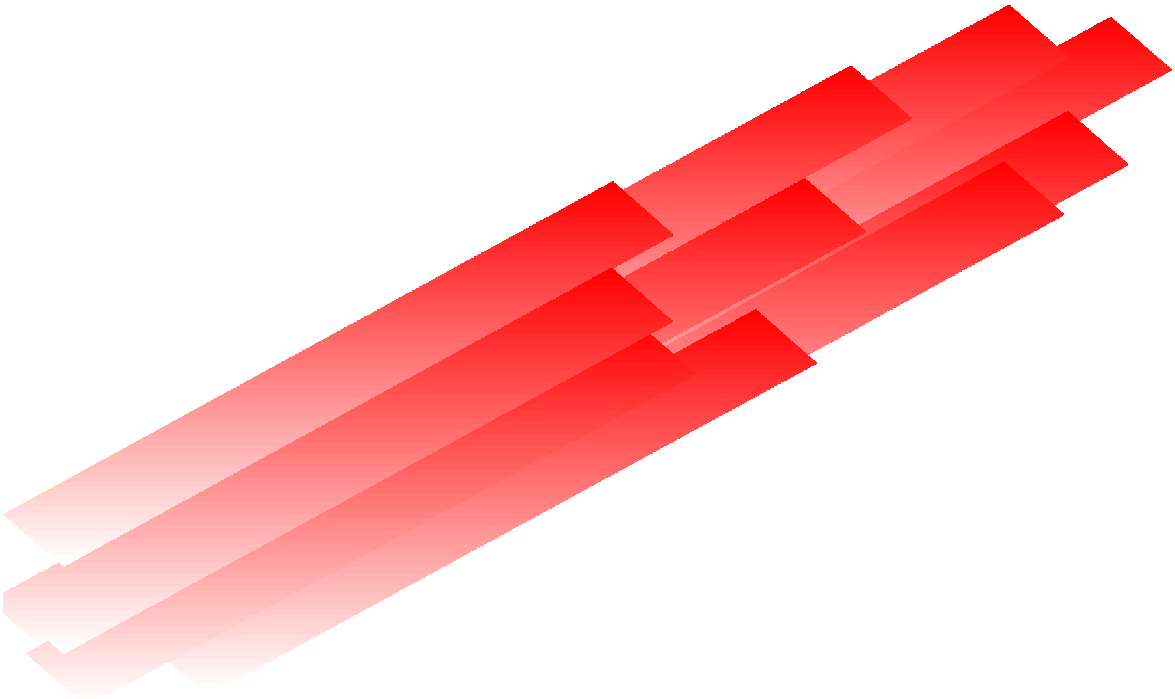
Guidance for Industry

Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug and Cosmetic Act



U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
June 1998

Procedural 6

Guidance for Industry

Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug and Cosmetic Act

Comments and suggestions regarding this document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the guidance. All comments should be identified with the docket number 98D-0265. Submit comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, Md. 20857.

After the comment period closes, comments should be provided in writing to the Center for Drug Evaluation and Research (CDER), Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20857; or Center for Biologics Evaluation and Research (CBER), 1401 Rockville Pike, Rockville, Md. 20852-1448.

Additional copies are available from:
The Drug Information Branch (HFD-210),Center for Drug Evaluation and Research (CDER),
5600 Fishers Lane, Rockville, MD 20857 (Tel) 301-827-4573
http://www.fda.gov/cder/guidance/index.htm
or
Office of Communication, Training, and Manufacturers Assistance (HFM-40),
Center for Biologics Evaluation and Research (CBER)
1401 Rockville Pike, Rockville, MD 20852-1448,
http://www.fda.gov/cber/guidelines.htm; (Fax) 888-CBERFAX or 301-827-3844
(Voice Information) 800-835-4709 or 301-827-1800

TABLE OF CONTENTS

GUIDANCE FOR INDUSTRY[1]

Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug and Cosmetic Act

I. WHY IS FDA ISSUING THIS GUIDANCE?

Section 111 of Title I of the Food and Drug Administration Modernization Act of 1997 (the Modernization Act), signed into law by President Clinton on November 21, 1997, created section 505A of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 355a). Section 505A permits certain applications to obtain an additional six months of exclusivity if, in accordance with the requirements of the statute, the sponsor submits requested information relating to the use of the drug in the pediatric population. The text of section 505A is reproduced at Attachment A. The Food and Drug Administration (FDA) plans to issue regulations through notice and comment rulemaking to implement the pediatric exclusivity provisions of the Modernization Act. The Agency is publishing this guidance to assist industry in interpreting section 505A in the interim. The guidance will be updated as appropriate. This guidance will remain in effect until superseded by regulations or new guidance.

This guidance describes how studies may qualify for pediatric exclusivity under section 505A. Topics covered include (1) whether studies for certain drugs will be requested under section 505A(a) or (c), (2) the definition of pediatric studies, (3) the content and format of an FDA request for pediatric studies, (4) how an applicant can obtain an FDA Written Request, (5) the content of a written agreement for the conduct of pediatric studies, (6) the definition of commonly accepted scientific principles, (7) the filing of reports of studies, (8) acceptance of studies by FDA, (9) scope and nature of pediatric exclusivity, (10) publication of exclusivity determinations, and (11) treatment of information submitted in support of a request for pediatric exclusivity.

---

[1]This guidance has been prepared by the Pediatric Exclusivity Working Group in the Center for Drug Evaluation and Research (CDER) in consultation with the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration. This guidance document represents the Agency's current thinking on the implementation of Section 111 of the Modernization Act and pediatric exclusivity. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

II. HOW DOES A NEW DRUG APPLICATION QUALIFY FOR PEDIATRIC EXCLUSIVITY?[2]

A. Prior to Approval of a New Drug Application (section 505A(a))

In general, for drugs that are not yet approved,[3] submission of reports of pediatric studies will qualify an application for pediatric exclusivity when all of the following have occurred:

1. The Agency must issue a Written Request for pediatric studies before the approval of a new drug application (NDA) submitted under section 505(b)(1) (21 U.S.C. 355(b)(1)).[4]

2. The reports of studies should be submitted after the Agency makes the Written Request.

3. Submitted studies must respond to the Written Request (section 505A(d)(2) and (3)).

4. Reports of the studies must be submitted in accordance with a written agreement (section 505A(d)(1) and (2)) or, if there is no written agreement, in accordance with commonly accepted scientific principles (section 505A(d)(3)).

5. The reports of the studies must be submitted in accordance with the Agency's requirements for filing (section 505A(d)).

6. The Agency must accept the reports of studies (section 505A(d)).

B. Approved New Drug Applications (section 505A(c))

In general, for drugs that are approved for adults and/or part of the pediatric population for an indication that occurs in the pediatric population, submission of reports of pediatric studies will qualify an application for pediatric exclusivity when all of the following have occurred:

---

[2]Consult individual sections of this guidance for additional information on each step.

[3]Studies in support of a pediatric use for a currently unapproved indication should be submitted as part of an application or supplement for approval of the indication, as described in this section.

[4]Applications submitted under section 505(b)(1) include full NDAs and 505(b)(2) applications. A 505(b)(2) application is a new drug application (NDA) submitted under section 505(b)(1) of the Act for which one or more of the investigations relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

1. The active moiety in the approved drug must appear on the "List of Approved Drugs for Which Additional Pediatric Information May Produce Health Benefits in the Pediatric Population" (section 505A(c)). Refer to Docket 98N-0056 for the current list of approved priority and nonpriority drugs.

2. The Agency must issue a Written Request for pediatric studies to the holder of an approved NDA after the application has been approved under section 505(b)(1).

3. The studies should be for pediatric use of the drug for an indication approved in adults and/or part of the pediatric population.

4. The holder of the approved application should submit the studies after the Agency has made the Written Request.

5. The submitted studies must respond to the Written Request (section 505A(d)(2) and (3)).

6. The holder of the approved application must submit reports of the studies in accordance with a written agreement (section 505A(d)(1) and (2)) or, if there is no written agreement, in accordance with commonly accepted scientific principles (section 505A(d)(3)).

7. The holder of the approved application must submit the reports of the studies in accordance with the Agency's requirements for filing (section 505A(d)).

8. The Agency must accept the reports of studies (section 505A(d)).

C. Antibiotics (previously submitted under old Section 507 of the Act)

An application for a drug that contains an antibiotic, in which the antibiotic was the subject of any application for marketing received before November 21, 1997 (hereinafter referred to as an "old" antibiotic), is not eligible to receive pediatric exclusivity unless (1) such antibiotic has or obtains orphan drug exclusivity under 527 of the Act and (2) the requirements for pediatric exclusivity are met. "Old" antibiotics are exempt from the exclusivity, patent listing, and patent certification provisions of section 505, and thus are not eligible for pediatric exclusivity that extends section 505 exclusivity, or that provides exclusivity at the end of the term of a listed patent. For further discussion of the current status of antibiotic drug applications and a list of "old" antibiotics, see FDA's Guidance *Repeal of Section 507 of the Federal Food, Drug, and Cosmetic Act.*

III. WHAT ARE PEDIATRIC STUDIES?

A. Definition of a Pediatric Study

The terms *pediatric studies* or *studies* are defined as at least one clinical investigation (that, at the Agency's discretion, may include pharmacokinetic studies) in pediatric age groups in which a drug is anticipated to be used (section 505A(g)).

B. Submission of Pediatric Study Protocols to an IND

Protocols for studies to obtain information relating to the use of a drug in the pediatric population should be submitted to an IND. Protocols to support studies for which pediatric exclusivity is sought should be identified with the header PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY.

C. Studies That May Be Used to Qualify for Pediatric Exclusivity

Studies submitted in response to the required Written Request may qualify an application to receive pediatric exclusivity. The party seeking exclusivity need not have conducted the studies it submits in response to a Written Request. Reports of studies conducted by someone other than the party requesting exclusivity should be submitted in response to a Written Request only if the studies meet the requirements of the Written Request. Data collected prior to or after FDA issues a Written Request may be used to respond to the request. FDA does not believe it would be consistent with the intent of the statute to accept data collected prior to the Written Request if such data are already known to provide no useful information. Therefore, FDA will not accept studies conducted prior to issuance of a Written Request unless the studies would potentially support a change to the label to incorporate pediatric information. Reviews of published literature are not pediatric studies that will qualify for pediatric exclusivity.

Studies submitted before FDA issued a Written Request should *not* be used to request pediatric exclusivity.

IV. WHAT IS AN FDA WRITTEN REQUEST FOR PEDIATRIC STUDIES?

A. Description of FDA's Written Request

For purposes of this guidance, a *request* is a specific document from FDA that is signed by the applicable Office Director and in which the Agency requests submission of certain studies to determine if the use of a drug could have meaningful health benefits in the pediatric population. FDA may issue a Written Request for those studies at the request of an interested party or on its own initiative. Issuance of a Written Request to a sponsor does not require the sponsor to conduct pediatric studies as described in the Written Request. It is the sponsor’s decision

whether to conduct the studies and possibly gain pediatric exclusivity. FDA's Written Request will include a provision for amending a Written Request.

Generally, FDA's request will address the following issues:

- Type of studies to be performed
- Objective/rationale
- Indication(s) to be studied
- Study design
- Age groups in which the studies will be performed
- Number of patients to be studied or power of the study to be achieved
- Entry criteria (i.e., inclusion/exclusion criteria)
- Clinical endpoints, if appropriate
  - noting proposed primary efficacy endpoint
- Study evaluations
- Drug information
  - dosage form
  - regimen(s)
  - route of administration
  - formulation
- Safety concerns
- Statistical information, including:
  - power of the study
  - statistical analyses of data to be performed
- Labeling that may result from the studies
- Format of report to be submitted to the Agency
- Timeframe for:
  - drafting the protocol(s)
  - submitting the protocol(s) to an investigational new drug application (IND)
  - enrolling study participants
  - completing study(ies)
  - drafting reports of the study(ies)
  - submitting reports of the study(ies)

The Agency may use a proposed pediatric study request to develop its Written Request or may use alternative information.

If an applicant believes it will be unable to meet the timeframe in a Written Request, it should contact FDA to request an extension for a timeframe as soon as possible. If FDA agrees to an extension, FDA will communicate the extension time in writing to the applicant in accordance with the provision for amending the Written Request.

B. Issuance of FDA's Written Request

All Written Requests ("Request for Pediatric Studies" letter) will be signed by the applicable Office Director in CDER or CBER.

1. Prior to approval of a drug, the Agency will make the Written Request to the sponsor of the NDA or, if there is no sponsor, may publish the Written Request in the *Federal Register*.[5]

2. For approved drugs, the Agency must issue the Written Request to the holder of the approved application(s) (section 505A(c)).

Agreements to perform Phase 4 studies or other communications concerning pediatric studies are *not* official requests as described in this guidance and required under the statute.

FDA will publish a list of approved drugs for which it has issued Written Requests.

V. HOW DO I OBTAIN A WRITTEN REQUEST?

A. Proposed Pediatric Study Requests From Interested Persons

To expedite the Agency's issuance of a Written Request, interested persons are strongly encouraged to submit proposed pediatric study requests to the appropriate new drug review division. Submitters should clearly mark proposals with the header PROPOSED PEDIATRIC STUDY REQUEST. Sponsors should plan to submit their proposed pediatric study request with sufficient time to permit FDA to review the proposed pediatric study request, confer with the sponsor as necessary, and issue a Written Request, and to permit sponsors to initiate, complete, and file reports of studies before expiry of a patent or exclusivity period.

At a minimum, any proposed pediatric study request should address the issues identified in section IV.A.

Proposed pediatric study requests should include the pediatric age groups in which particular drug products will be studied. The pediatric age groups for the purpose of studies are defined as neonate (birth to 1 month), infant (1 month to 2 years), child (2 to 12 years), and adolescent (12 years to <16 years). FDA understands that certain drugs are more appropriately studied in groups categorized by the maturity of certain biological processes (e.g., onset of puberty). If data are submitted as part of a proposed pediatric study request to indicate that a drug should be studied in pediatric groups identified by characteristics other than age, FDA will consider the data in composing its Written Request. FDA will also consider requests to study multiple pediatric age

[5]The Agency could publish a Written Request if, for example, it believed that information on the pediatric use of a drug for an unapproved indication would provide health benefits in the pediatric population, it sought pediatric studies related to approval of the indication, and it had not received an application for that indication.

groups in the same study, if appropriate. In submitting proposed pediatric study requests, sponsors should consider which age groups may obtain the greatest health benefits from additional pediatric information.

B. FDA Prioritization and Processing of Proposed Pediatric Study Requests

Sponsors of applications for approved drugs that appear in the priority section of the list (see Docket No. 98N-0056) for which any exclusivity or patent period expires on or before March 31, 1999, should submit proposed pediatric study requests to the appropriate new drug review division with a facsimile copy to Ms. Khyati Roberts, HFD-6, (301) 594-5493(f) on or before August 31, 1998, for expedited consideration. These sponsors should label their proposals PROPOSED PEDIATRIC STUDY REQUEST - EXPIRATION ON OR BEFORE MARCH 31, 1999. FDA will endeavor to issue Written Requests on or before October 15, 1998, for adequate proposals or as soon thereafter as possible. FDA will ask sponsors of proposals that are submitted before August 31, 1998, and that are not adequate to resubmit their proposal. The resubmitted proposal will be processed based on the date of resubmission. Other proposed pediatric study requests may also be submitted during this period but will be processed in the order described in this section.

Generally, FDA will process proposed pediatric study requests as a first, second, third, or fourth priority as described in the following table:

	Drugs on the Priority Section of the List		**Drugs Not on the Priority Section of the List**		**Unapproved Drugs**
	Patent or Exclusivity expiration on or before 03/31/99	Patent or Exclusivity expiration *not* on or before 03/31/99	Patent or Exclusivity expiration on or before 03/31/99	Patent or Exclusivity expiration *not* on or before 03/31/99	
Proposed Pediatric Study Request submitted on or before 08/31/98	1	2	3	4	2
Proposed Pediatric Study Request *not* submitted on or before 08/31/98	2		4		2

This means:

1. FDA will first review proposed pediatric study requests submitted on or before August 31, 1998, for approved drugs that appear in the priority section of the list for which any exclusivity or patent period expires on or before March 31, 1999.

2. FDA will next review:

a. any other proposed pediatric study requests for approved drugs that appear in the priority section of the list, and

b. proposed pediatric study requests submitted for drugs that are not yet approved.

3. FDA will then review proposed pediatric study requests submitted on or before August 31, 1998, for approved drugs that appear in the nonpriority section of the list for which any exclusivity or patent period expires on or before March 31, 1999.

4. FDA will finally review any other proposed pediatric study requests for approved drugs that appear in the nonpriority section of the list.

Generally, FDA will review proposed pediatric study requests within each priority in the order the proposals are received by the appropriate new drug review division as indicated by the official FDA document room receipt stamp.

As FDA gains experience with this process, it may provide additional guidance regarding the timing of a proposed pediatric study request.

C. Changes to the List of Approved Drugs for Which Additional Pediatric Information May Produce Health Benefits in the Pediatric Population

Persons may request changes to the list, including the addition of a drug to the priority section of the list, by submitting a citizen petition under 21 CFR 10.30. Petitioners should include in the header of the petition PEDIATRIC PRIORITY LIST so that their petition can be distinguished from other types of citizen petitions and be accorded special handling.

Drugs are included in the priority section of the list if:

- The drug product, if approved for use in the pediatric population, would be a significant improvement compared to marketed products labeled for use in the treatment, diagnosis, or prevention of a disease in the relevant pediatric population (i.e., a pediatric priority drug); or,

- The drug is widely used in the pediatric population, as measured by at least 50,000 prescription mentions per year; or,

- The drug is in a class or for an indication for which additional therapeutic or

diagnostic options for the pediatric population are needed.[6]

VI. WHAT IS THE CONTENT OF A WRITTEN AGREEMENT FOR THE CONDUCT OF PEDIATRIC STUDIES?

FDA recommends that persons to whom Written Requests are issued reach a signed written agreement with FDA for the conduct of pediatric studies. The written agreement should address all of the items in the Written Request. In addition, the agreement should outline what will be necessary to meet the study objective(s). The agreement should state that the results of the study as conducted are to adequately address the objective of the study as set forth in the Written Request (section 505A(d)).

The written agreement should include the protocol for the study to be conducted or procedures for review of the protocol. The protocol should meet the requirements of 21 CFR 312.23(a)(6). Where required, adequate and well-controlled studies should meet the requirements of 21 CFR 314.126.

A written agreement for the conduct of pediatric studies may be modified by written agreement between the Agency and the sponsor.

VII. WHAT ARE COMMONLY ACCEPTED SCIENTIFIC PRINCIPLES AND PROTOCOLS?

Over the years, FDA has strived to put in writing commonly accepted scientific principles. FDA's regulations and guidances should serve as a source of information and standards for those seeking to write protocols and to use commonly accepted scientific principles of study design, conduct, and analysis. In particular, FDA recommends a review of:

---

[6]FDA compiled an initial working list based on recommendations from the American Academy of Pediatrics, the Pharmaceutical Research and Manufacturers Association, the National Institutes of Health, the Pediatric Pharmacology Research Units Network, the National Pharmaceutical Alliance, the Generic Pharmaceutical Industry Association, the National Association of Pharmaceutical Manufacturers, and the United States Pharmacopeia. FDA also included on this initial working list drugs identified in the Orange Book as having remaining patent and/or exclusivity life. After internal review of this working list, FDA published a draft list on March 16, 1998 (63 FR 12815).

After consideration of comments received on the draft list, FDA concluded that information on any drug approved for an indication that occurs in the pediatric population may produce health benefits in the pediatric population. Therefore, all drugs approved by CDER and CBER that are approved for indications that occur in children are considered to be on the list. In considering alternative approaches to establishing priorities among the drugs on the draft list, FDA concluded that the criteria used to include drugs on the draft list best describe those drugs for which studies would be considered a high priority because they might provide a significant benefit to the pediatric population. These criteria are described in this guidance. The Agency included the drugs that met the criteria on the priority section of the list.

- § 312.23 (describing protocol contents),
- § 314.126 (describing adequate and well-controlled studies),

and the guidances:

- *ICH E3: Structure and Content of Clinical Study Reports* (July 1996),
- *ICH E4: Dose-Response Information to Support Drug Registration*,
- *ICH E6: Good Clinical Practices: Consolidated Guideline* (May 1997),
- *ICH E8: General Considerations for Clinical Trials* (December 1997),
- *Content and Format for Pediatric Use Supplements*, and
- *Format and Content of Clinical and Statistical Sections of New Drug Applications* (July 1988).

FDA plans to use its regulations and guidances to determine whether submitted studies were conducted in accordance with commonly accepted scientific principles and protocols, as required under section 505A(d)(3).

To avoid confusion, FDA recommends that an interested party reach a written agreement with FDA before developing pediatric studies rather than seek an FDA finding that studies were conducted in accordance with commonly accepted scientific principles and protocols after the study was conducted.

VIII. HOW DO I FILE MY REPORTS OF STUDIES WITH FDA?

Sections 505A(d)(2) and (3) require reports of studies to be submitted in accordance with FDA's requirements for filing. The term *filing* has a specific legal meaning under the Act (see 21 U.S.C. 355, 21 CFR 314.101). Accordingly, to file reports of studies, an applicant should submit a supplement or a new drug application in accordance with the regulatory requirements for filing such documents. A supplement generally would be for a change in an approved product's labeling designed to incorporate information obtained from the pediatric studies. The supplement or NDA containing the reports of pediatric studies need not obtain approval in order for the reports of studies to be accepted by FDA and qualify an application to receive pediatric exclusivity.

Reports of studies completed under protocols submitted to an IND must be submitted in accordance with 21 CFR 314.50 and should be submitted in accordance with the *Guidelines for Format and Content of Clinical and Statistical Sections of New Drug Applications* (July 1988) and *ICH E3: Structure and Content of Clinical Study Reports* (July 1996).

To ensure that reports of pediatric studies are evaluated for eligibility for pediatric exclusivity in a timely manner, an applicant should include with the application or supplement:

- A header on the cover sheet that states: SUBMISSION OF PEDIATRIC STUDY

REPORTS -- PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED

- A copy of the Written Request
- A copy of any written agreement

Applicants should send a facsimile copy of the cover sheet to the Office of Generic Drugs (OGD), FDA, Attn: Director, OGD (HFD-600), (301) 594-0183(f).

IX. WHAT CONSTITUTES ACCEPTANCE OF MY REPORTS OF STUDIES?

A. Definition of Acceptance

Acceptance means the Agency has determined that the studies were conducted in accordance with the original Written Request and either a written agreement if one existed or commonly accepted scientific principles if no written agreement existed, and were reported in accordance with FDA's requirements for filing (section 505A(d)(2) and (3)).

B. Notification of Acceptance

A sponsor who had a written agreement with FDA will be notified whether the sponsor's reports of studies qualified for pediatric exclusivity by CDER or CBER, as appropriate, before the expiration of the 60-day period after the sponsor submitted the reports of studies (section 505A(d)(2)).

A sponsor who did not have a written agreement with FDA will be notified whether the sponsor's reports of studies qualified for pediatric exclusivity by CDER or CBER, as appropriate, before the expiration of the 90-day period after the sponsor submitted the reports of studies (section 505A(d)(3)).

X. IF MY STUDY QUALIFIES FOR PEDIATRIC EXCLUSIVITY, TO WHAT WILL THE PERIOD OF PEDIATRIC EXCLUSIVITY ATTACH?

A. Pediatric Exclusivity

Pediatric exclusivity will attach to any exclusivity or patent protection that is, or will be, listed in the *Orange Book* for any drug product containing the same active moiety as the drug studied and for which the party submitting the studies holds the approved new drug application (505A(a) and(c)). Pediatric exclusivity extends any exclusivity and patent protection the drug product has by a period of six months. For example, if the drug product has five-year, new chemical entity exclusivity, the addition of pediatric exclusivity will give the applicant five and one half years of new chemical entity exclusivity. Pediatric exclusivity attaching to the end of a patent term is not a patent term extension under 35 U.S.C. 156. Rather, it extends the period during which an ANDA or 505(b)(2) application may not be approved by FDA.

B. Multiple Six-Month Periods of Pediatric Exclusivity

A second pediatric study meeting the statutory requirements described in this guidance and submitted in a supplemental application for a drug that has already received one period of pediatric exclusivity may qualify the drug to receive one additional period of exclusivity. The one additional period of pediatric exclusivity will attach only to any exclusivity period under sections 505(c)(3)(D)(iii) and (iv) and 505(j)(5)(D)(iii) and (iv).

XI. PUBLICATION OF PEDIATRIC EXCLUSIVITY DETERMINATIONS

Pediatric exclusivity information will be published in the "Patent and Exclusivity Information" section of the *Orange Book* and its supplements in the same manner as Waxman-Hatch exclusivity, patent listings, and orphan drug exclusivity are currently published.

XII. HOW WILL FDA TREAT INFORMATION SUBMITTED IN SUPPORT OF A REQUEST FOR PEDIATRIC EXCLUSIVITY?

If FDA finds that a significant number of applications are obtaining pediatric exclusivity without the useful information derived from the studies being announced through labeling changes, FDA will consider appropriate methods for making the information publicly available so as to benefit the pediatric population.

ATTACHMENT A - SECTION 111 OF THE MODERNIZATION ACT
21 USC 355a (1997)

§ 355a. Pediatric studies of drugs

(a) MARKET EXCLUSIVITY FOR NEW DRUGS. If, prior to approval of an application that is submitted under section 505(b)(1), the Secretary determines that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), and such studies are completed within any such timeframe and the reports thereof submitted in accordance with subsection (d)(2) or accepted in accordance with subsection (d)(3)--

(1) (A) (i) the period referred to in subsection (c)(3)(D)(ii) of section 505, and in subsection (j)(4)(D)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(D)(ii) and (j)(4)(D)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(ii) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(D) of such section, and in clauses (iii) and (iv) of subsection (j)(4)(D) of such section, is deemed to be three years and six months rather than three years; and

(B) if the drug is designated under section 526 for a rare disease or condition, the period referred to in section 527(a) is deemed to be seven years and six months rather than seven years; and

(2) (A) if the drug is the subject of--

(i) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(ii) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(B) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(b) SECRETARY TO DEVELOP LIST OF DRUGS FOR WHICH ADDITIONAL PEDIATRIC INFORMATION MAY BE BENEFICIAL. Not later than 180 days after the date of enactment of the Food and Drug Administration Modernization Act of 1997, the Secretary,

after consultation with experts in pediatric research shall develop, prioritize, and publish an initial list of approved drugs for which additional pediatric information may produce health benefits in the pediatric population. The Secretary shall annually update the list.

(c) MARKET EXCLUSIVITY FOR ALREADY-MARKETED DRUGS. If the Secretary makes a written request to the holder of an approved application under section 505(b)(1) for pediatric studies (which shall include a timeframe for completing such studies) concerning a drug identified in the list described in subsection (b), the holder agrees to the request, the studies are completed within any such timeframe, and the reports thereof are submitted in accordance with subsection (d)(2) or accepted in accordance with subsection (d)(3)--

(1) (A) (i) the period referred to in subsection (c)(3)(D)(ii) of section 505, and in subsection (j)(4)(D)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(D)(ii) and (j)(4)(D)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(ii) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(D) of such section, and in clauses (iii) and (iv) of subsection (j)(4)(D) of such section, is deemed to be three years and six months rather than three years; and

(B) if the drug is designated under section 526 for a rare disease or condition, the period referred to in section 527(a) is deemed to be seven years and six months rather than seven years; and

(2) (A) if the drug is the subject of--

(i) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(ii) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(B) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(d) CONDUCT OF PEDIATRIC STUDIES.

(1) Agreement for studies. The Secretary may, pursuant to a written request from the Secretary under subsection (a) or (c), after consultation with--

(A) the sponsor of an application for an investigational new drug

under section 505(i);

(B) the sponsor of an application for a new drug under section 505(b)(1); or

(C) the holder of an approved application for a drug under section 505(b)(1),

agree with the sponsor or holder for the conduct of pediatric studies for such drug. Such agreement shall be in writing and shall include a timeframe for such studies.

(2) Written protocols to meet the studies requirement. If the sponsor or holder and the Secretary agree upon written protocols for the studies, the studies requirement of subsection (a) or (c) is satisfied upon the completion of the studies and submission of the reports thereof in accordance with the original written request and the written agreement referred to in paragraph (1). Not later than 60 days after the submission of the report of the studies, the Secretary shall determine if such studies were or were not conducted in accordance with the original written request and the written agreement and reported in accordance with the requirements of the Secretary for filing and so notify the sponsor or holder.

(3) Other methods to meet the studies requirement. If the sponsor or holder and the Secretary have not agreed in writing on the protocols for the studies, the studies requirement of subsection (a) or (c) is satisfied when such studies have been completed and the reports accepted by the Secretary. Not later than 90 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary's only responsibility in accepting or rejecting the reports shall be to determine, within the 90 days, whether the studies fairly respond to the written request, have been conducted in accordance with commonly accepted scientific principles and protocols, and have been reported in accordance with the requirements of the Secretary for filing.

(e) DELAY OF EFFECTIVE DATE FOR CERTAIN APPLICATION. If the Secretary determines that the acceptance or approval of an application under section 505(b)(2) or 505(j) for a new drug may occur after submission of reports of pediatric studies under this section, which were submitted prior to the expiration of the patent (including any patent extension) or the applicable period under clauses (ii) through (iv) of section 505(c)(3)(D) or clauses (ii) through (iv) of section 505(j)(4)(D), but before the Secretary has determined whether the requirements of subsection (d) have been satisfied, the Secretary shall delay the acceptance or approval under section 505(b)(2) or 505(j) until the determination under subsection (d) is made, but any such delay shall not exceed 90 days. In the event that requirements of this section are satisfied, the applicable six-month period under subsection (a) or (c) shall be deemed to have been running during the period of delay.

(f) NOTICE OF DETERMINATIONS ON STUDIES REQUIREMENT. The Secretary shall publish a notice of any determination that the requirements of subsection (d) have been met and that submissions and approvals under subsection (b)(2) or (j) of section 505 for a drug will be subject to the provisions of this section.

(g) DEFINITIONS. As used in this section, the term "pediatric studies" or "studies" means at least one clinical investigation (that, at the Secretary's discretion, may include pharmacokinetic studies) in pediatric age groups in which a drug is anticipated to be used.

(h) LIMITATIONS. A drug to which the six-month period under subsection (a) or (b) has already been applied--

(1) may receive an additional six-month period under subsection (c)(1)(A)(ii) for a supplemental application if all other requirements under this section are satisfied, except that such a drug may not receive any additional such period under subsection (c)(2); and

(2) may not receive any additional such period under subsection (c)(1)(B).

(i) RELATIONSHIP TO REGULATIONS. Notwithstanding any other provision of law, if any pediatric study is required pursuant to regulations promulgated by the Secretary and such study meets the completeness, timeliness, and other requirements of this section, such study shall be deemed to satisfy the requirement for market exclusivity pursuant to this section.

(j) SUNSET. A drug may not receive any six-month period under subsection (a) or (c) unless the application for the drug under section 505(b)(1) is submitted on or before January 1, 2002. After January 1, 2002, a drug shall receive a six-month period under subsection (c) if--

(1) the drug was in commercial distribution as of the date of enactment of the Food and Drug Administration Modernization Act of 1997;

(2) the drug was included by the Secretary on the list under subsection (b) as of January 1, 2002;

(3) the Secretary determines that there is a continuing need for information relating to the use of the drug in the pediatric population and that the drug may provide health benefits in that population; and

(4) all requirements of this section are met.

(k) REPORT. The Secretary shall conduct a study and report to Congress not later than January 1, 2001, based on the experience under the program established under this section. The study and report shall examine all relevant issues, including--

(1) the effectiveness of the program in improving information about important pediatric uses for approved drugs;

(2) the adequacy of the incentive provided under this section;

(3) the economic impact of the program on taxpayers and consumers, including the impact of the lack of lower cost generic drugs on patients, including on lower income patients; and

(4) any suggestions for modification that the Secretary determines to be appropriate.

HISTORY: (June 25, 1938, ch 675, Ch V, § 505A, as added Nov. 21, 1997, P.L. 105-115, Title I, Subtitle B, § 111, 111 Stat. 2305.)